

Attachment to Amendment and Reply dated

Marked-up Claim 14

14. (Twice Amended) A method for categorizing nucleic acid, wherein said method comprises:

(i) digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population, wherein said endonuclease is selected such that each nucleic acid in the resulting nucleic acid population has a sticky end of a known base sequence and of a known common length extending from a terminal of its double-stranded portion, and wherein each nucleic acid in the nucleic acid population has a double-stranded portion;

(ii) contacting the nucleic acid population with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein said adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population;

(iii) categorizing the nucleic acid by isolating [a] nucleic [acid] acids wherein both termini of the double-stranded portion of said nucleic acid correctly hybridize to an oligonucleotide sequence by contacting a first set of oligonucleotide sequences with the nucleic acid population by:

(a) denaturing the nucleic acid population in the presence of the first set of oligonucleotide sequences covalently linked to a solid phase support to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first set of oligonucleotide sequences, wherein each oligonucleotide sequence in said

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first set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

(b) immobilizing those nucleic acids which correctly hybridise to the oligonucleotide sequence added to that well;

(c) extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid;

(d) denaturing the double-stranded nucleic acid and removing non-immobilised species to isolate the resulting immobilised single-stranded nucleic acid;

(e) contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences, wherein each oligonucleotide sequence in said second set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

(f) extending the correctly hybridised oligonucleotide sequences along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid;

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- (g) denaturing the double-stranded nucleic acid; and
- (h) isolating the resulting non-immobilised single-stranded nucleic acid.